REMARKS

Claims 1-44 are currently pending in the present application. By the present amendment, claim 11 has been canceled, and claims 45-49 have been added. The applicants have added eight new claims and canceled one claim. The applicants enclose a fee of $63.00 for the seven additional claims over 20 that were added.

Support for the amended and newly added claims is as follows. Support for amended claims 1-2, 22, 25, 28 and 41 can be found in the application at pp. 12-13 and original claim 11. Support for amended claim 27 can be found at p. 12, ll. 5-12 and p. 26, ll. 1-9. Support for amended claims 29 and 42 can be found at pp. 12-13, the paragraph beginning at p. 22, ll. 28, and the working examples (pp. 25-31). Support for newly added claims 45-51 can be found at p. 12, ll. 13-16, and the working examples, and in particular the Y-HK polymer described in section 6.4.10 (p. 29, ll. 7-15). Support for newly added claim 52 can be found at p. 12, ll. 5-12. Applicant notes that claim 1 was amended to recite at least 10% non-histidine residues in order to more clearly indicate that the scope of the claim does not read on peptides consisting only of histidine. All other amendments were made to claim preferred embodiments of the present invention.

Claims 1-2, 4-13 and 15-44 stand rejected under 35 U.S.C. 112, first paragraph, as lacking written description support. Claims 1-2, 4-13 and 15-44 stand rejected under 35 U.S.C. 112, first paragraph, as lacking enablement support. Claims 1-2, 4, 7-13, 15, 18-25, 27-31, and 34-43 stand rejected under 35 U.S.C. 102(e) as being anticipated by PACK et al. (US 2001/0006817 A1). Claims 1, 2, 4-13, 15-44 stand rejected under 35 U.S.C. 103(a) as being unpatentable over PACK et al. taken with either Hawley-Nelson (USPN 6,051,429) or Tomalia (USPN 6,475,994). Claims 1, 2, 4-13, 15-44 stand rejected under 35 U.S.C. 103(a) as being unpatentable over PACK et al. taken with either Hawley-Nelson (USPN 6,051,429) or Tomalia (USPN 6,475,994), and further in view of Gopal. Applicant respectfully traverses these rejections.

Written Description Rejection

Claims 1-2, 4-13 and 15-44 stand rejected under 35 U.S.C. 112, first paragraph, as lacking written description support.

Claim 1 as originally filed (and currently amended) is directed to a pharmaceutical agent delivery composition comprising a transport polymer and an associated pharmaceutical agent. Claim 27 as originally filed (and currently amended) optionally comprises in addition an intracellular delivery component. Claim 1 as currently amended and claim 27 as originally filed (and currently amended) further recite that the transport polymer comprise a peptide having a minimum specified number of amino acid residues, of which at least 10% are histidine and at least 10% are non-histidine. That all of the structural limitations recited in the claims for the peptide component of the transport polymer find literal support in the application as filed is beyond argument. See specifically, pp. 12-13 and claims in the originally filed application. Furthermore, it is beyond argument that the skilled artisan could envision all of the possible peptides recited in the claims. For example, a linear peptide of length X consisting of naturally occurring amino acids defines a genus of peptides having X^{20} possible amino acid sequences.[1] There is no question that a skilled artisan could readily identify each and every species falling within this genus which has at least 10% histidine and at least 10% non-histidine residues. Similarly, a skilled artisan could readily identify each and every branched peptide meeting the structural limitations recited in the claims.

Notwithstanding the ability of the skilled artisan to recognize all of the species of peptides called for in the claims, the Examiner has taken the position that the claims fail to recite "essential or critical elements which are not adequately described in the specification and which is not conventional in the art as of applicants effective filing date." According to the Examiner:

> Claiming a genus of an enormous number of transport polymers, with a mere description of the presence of at least 10% histidine residues being present, without a description of a common structure of the essential domain of the transport polymer in order to carryout the transporting property as contemplated by applicant's disclosure without defining what means will do so is not in compliance with the written description requirement.

Applicant respectfully disagrees with the Examiner. The specification teaches that the property of enhanced transport of pharmaceutical agents is the result of the presence of a histidine component in the transport polymer. See p. 22, ll. 18-23; p. 27, ll. 18-30; p. 28, l. 31 – p. 29, l. 6. The specification further teaches by working examples that enhanced transport can be achieved regardless of the size of the peptide (p. 26, ll. 1-9); regardless of the non-histidine component of

[1] Applicant notes that the claims are not restricted to naturally occurring amino acids. See p. 9, ll. 17-19 of the present application.

the peptide (p. 27, ll. 18-30); regardless of whether the peptide is linear or branched (p. 26, ll. 10-16); regardless of the peptide concentration (p. 25, ll. 18-34); regardless of the percentage of the peptide which is histidine (p. 29, ll. 6-23); and regardless of the histidine order within the peptide (p. 29, ll. 6-23). While the specification clearly teaches that each of these parameters can affect the degree of enhancement in transport, such teachings do not diminish the general teaching of the specification that enhanced transport is achieved by incorporating histidine into the peptide component of the transport polymer.

In its Guidelines, the PTO has determined that the written description requirement for a claimed genus can be met by "sufficient description of a representative number of species by actual reduction to practice ..., reduction to drawings ..., or by disclosure relevant, identifying characteristics, *i.e.*, structure [complete or partial] or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus." Guidelines, 66 Fed. Reg. at 1106. (See also Enzo Biochem v. Gen-Probe, Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002) (giving judicial notice to the PTO's written description guidelines published in the Federal Register to the extent they do not conflict with the statute.) In the present case, the specification not only describes the claimed genus literally and provides a number of working examples, but also teaches a correlation between function (enhanced transport) and a common structural feature (presence of histidine). Accordingly, the skilled artisan would clearly recognize that applicant was in possession of the claimed pharmaceutical agent delivery compositions.

For the same reasons as noted above for claims 1 and 27, claims 2, 4-10, 28-39, 45-48, 50 and 52, which depend therefrom, have adequate written description support. Similarly, because claims 25-26, directed to a method of producing a pharmaceutical agent delivery system, comprise a step of providing a transport polymer comprising a peptide having the same limitations recited in claim 1, claims 25-26 have adequate written description support. Finally, the specification teaches methods for delivering a pharmaceutical agent to the interior of a cell using the claimed pharmaceutical agent delivery compositions. See p. 20, l. 24 – p. 21, l. 16 and working examples. The methods described encompass *in vitro, in vivo* and *ex vivo* approaches. Accordingly, claims 12-13, 15-24, 40-44, 49 and 51 have adequate written description support.

For the reasons stated above, applicant respectfully requests withdrawal of the written description rejection.

Enablement Rejection

Claims 1-2, 4-13 and 15-44 stand rejected under 35 U.S.C. 112, first paragraph, as lacking enablement support. Specifically, the Examiner states that:

> Since the claimed invention is not supported by a sufficient written description (for possessing [sic] of the genus of polymeric transporting complexes as recited in the claims, ... one skilled in the art would not know how to use and make the claimed invention so that it would operate as intended.

Applicants respectfully traverse this rejection. As noted above, the specification provides adequate written description support for all of the currently pending claims, including newly added claims 45-52. Because the Examiner has not provided any other reasonable basis to question the enablement provided for the claimed invention, applicant respectfully requests withdrawal of the enablement rejection.

Prior Art Rejections

Claims 1-2, 4, 7-13, 15, 18-25, 27-31, and 34-43 stand rejected under 35 U.S.C. 102(e) as being anticipated by PACK et al. (US 2001/0006817 A1). Claims 1, 2, 4-13, 15-44 stand rejected under 35 U.S.C. 103(a) as being unpatentable over PACK et al. taken with either Hawley-Nelson (USPN 6,051,429) or Tomalia (USPN 6,475,994). Claims 1, 2, 4-13, 15-44 stand rejected under 35 U.S.C. 103(a) as being unpatentable over PACK et al. taken with either Hawley-Nelson (USPN 6,051,429) or Tomalia (USPN 6,475,994), and further in view of Gopal.

While not necessarily agreeing with the Examiner's determination that PACK et al. anticipates the presently claimed invention, or that PACK et al. when combined with the other cited references render obvious the claimed invention, applicant submits herewith a 37 C.F.R. 1.131 declaration which antedates PACK et al. The declaration by the above named inventor establishes that a species falling within the alleged genus of histidine and lysine copolymers disclosed by PACK et al. was reduced to practice prior to earliest effective filing date of the PACK et al. Because the species reduced to practice provides an adequate basis for inferring that copolymers of histidine and lysine can be used to increase the intracellular delivery of DNA,

applicant has demonstrated prior reduction to practice of as much of the claimed invention as PACK et al. is alleged to show. See *Ex parte Biesecker*, 144 USPQ 129 (Bd. App. 1964); *In re Mantell* 172 USPQ 530 (CCPA 1973); *In re Schaub*, 190 USPQ 324 (CCPA 1976).

Since PACK et al. is removed as a reference, applicant respectfully requests that all prior art rejections be withdrawn.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance; however, if the Examiner disagrees, the applicants respectfully request that the Examiner telephone the undersigned at (302) 888-6210.

A one month extension fee has been paid. Applicant notes that a one month extension of the original three month period, which ended 4/29/04, makes this response timely if filed on or before June 1, 2004, since the last day for response is Saturday 5/29/04 and Monday (5/31/04) is a Federal holiday. A fee for additional claims over 20 has also been made. If there are any additional fees due in connection with the filing of this response, including any fees required for an additional extension of time under 37 CFR 1.136, such an extension is requested and the Commissioner is authorized to charge any debit or credit any overpayment to Deposit Account No. 03-2775, under Order No. 05627-00005-USA from which the undersigned is authorized to draw.

Dated: June 1, 2004

Respectfully submitted,

By Gary A. Bridge

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